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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,082	08/26/2003	Philip Dehayza	2055/100F558-US2	4920

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EXAMINER	
JONES, DWAYNE C	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,082	DEHAYZA ET AL.	
	Examiner	Art Unit	
	Dwayne C Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-17 are pending.

2. Claims 1-17 are rejected.

Response to Arguments

3. Applicants' arguments filed November 5, 2004 have been fully considered but they are not persuasive. Applicants present the following arguments. First, applicants submit the rejection of June 3, 2004 concedes that Pouyani et al. do not teach of microspheres composed of hyaluronic acid functionalized with dihydrazide. Second, applicants allege that Kyyronen et al. is silent on hyaluronic acid functionalized with hydrazide. Third, applicants purport that there is no suggestion or motivation in either of these prior art references for one of ordinary skill in the art to combine these references to arrive a the instantly claimed subject matter.

4. First, applicants submit the rejection of June 3, 2004 concedes that Pouyani et al. do not teach of microspheres composed of hyaluronic acid functionalized with dihydrazide. It is first noted that the rejection is not over Pouyani et al. by itself but rather over Pouyani et al. in view of Kyyronen et al. For this reason, Kyyronen et al. do provide the skilled artisan with the explicit teaching of using hyaluronic acid derivatives as microspheres. In addition, Kyyronen et al. specifically teach and disclose of using the microspheres of hyaluronic acid derivatives to deliver pharmaceuticals, (see column 1, page 162). Pouyani et al. disclose that the functionalized derivatives of hyaluronate

that are cross-linked with a dihydrazide while in the presence of a carbodiimide, (see Scheme 1, column 4, liens 30-41). Moreover, Pouyani et al. also teach that the pore size of the hyaluronic acid functionalized with dihydrazide matrix ranges from 20 μm to 100 μm (see column 33, Example 8), while the pore size of the hyaluronic acid functionalized with dihydrazide matrix of the instantly claimed subject matter ranges from about 1 μm to about 500 μm. Not only does the prior art reference of Pouyani et al. teach of the same functionalized hyaluronic acid matrix, but there is also an overlap in the ranges of the pore sizes of the claimed subject matter and Pouyani et al, which reinforces the obviousness rejection of record. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA1976); *In re Woodruff*, 919 F.2d 1517, 16 USPQ2d 1934 (Fed. Cir. 1990).

5. Second, applicants allege that Kyyronen et al. is silent on hyaluronic acid functionalized with hydrazide. As previously stated, although for the prior art reference of Pouyani et al., the rejection is not over Kyyronen et al. by itself but rather over Pouyani et al. in view of Kyyronen et al. For this reason, Kyyronen et al. do provide the skilled artisan with the explicit teaching of using hyaluronic acid derivatives as microspheres along with the teachings of Pouyani et al. In addition, Kyyronen et al. specifically teach and disclose of using the microspheres of hyaluronic acid derivatives to deliver pharmaceuticals, (see column 1, page 162).

6. Third, applicants purport that there is no suggestion or motivation in either of these prior art references for one of ordinary skill in the art to combine these references

to arrive a the instantly claimed subject matter. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Pouyani et al. disclose of a process to functionalized the hyaluronate by reacting hyaluronate with a dihydrazide while in the presence of carbodiimide, (see Scheme 1, column 4, lines 30-41). Pouyani et al. do not specifically teach of microspheres of hyaluronic acid; however, Pouyani et al. do state that functionalized hyaluronic acid compositions can be thought of as being composed of hydrophilic monomer units linked to form a soluble polymeric network and eventually crosslinked to form an insoluble network and that functionalized hyaluronic acid possesses a number of characteristics that make it advantageously used as a carrier of drugs, (see column 3, lines 44-51 and lines 60-65). The prior art reference of Kyyronen et al. teach of derivative microspheres of hyaluronic acid that are used to deliver a pharmaceutical, namely hydrocortisone, (see column 1, page 162). In addition, it is noted that the instant claims are only directed to composition claims that require a microsphere comprised of hyaluronic acid that is derivatized with a crosslinker of dihydrazide, which is even activated with a carbodiimide. Furthermore, the instant

rejection under 103(a) over Pouyani et al. in view of Kyyronen et al. also teach of the claimed subject matter and so accordingly render the instant claims obvious.

Claim Rejections - 35 USC § 112

7. The rejection of claims 1, 6-13, and 15-17 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for functionalized hyaluronic acids with the crosslinker of a dihydrazide of the formula of claims 2 and 14, does not reasonably provide enablement for other types of derivatives of functionalized hyaluronic acids, including functionalized hyaluronic acids with other crosslinking agents is removed in response to the amendment of November 5, 2004.

8. The rejection of claims 1, 6-10, and 15-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is removed in response to the amendment of November 5, 2004.

9. The rejection of claims 1, 4, and 15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is removed in response to the amendment of November 5, 2004.

Claim Rejections - 35 USC § 102

10. The rejection of claims 1 and 7 under 35 U.S.C. 102(b) as being clearly anticipated by Illum of U.S. Patent No. 5,690,954 is removed in response to the amendment of November 5, 2004.

11. The rejection of claims 1 and 7 under 35 U.S.C. 102(b) as being clearly anticipated by Kyyronen et al. is removed in response to the amendment of November 5, 2004.

12. The rejection of claim 6 under 35 U.S.C. 102(b) as being clearly anticipated by Illum of U.S. Patent No. 5,690,954 is removed in response to the amendment of November 5, 2004.

13. The rejection of claim 6 under 35 U.S.C. 102(b) as being clearly anticipated by Kyyronen et al. is removed in response to the amendment of November 5, 2004.

Claim Rejections - 35 USC § 103

14. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

15. The rejection of claims 1-17 under 35 U.S.C. 103(a) as being unpatentable over Pouyani et al. of U.S. Patent No. 5,616,568 in view of Kyyronen et al. is maintained and repeated for both the above-stated and reasons of record. Pouyani et al. teach of functionalized derivatives of hyaluronate that are cross-linked and are used to therapeutically deliver biological compounds, such as anti-infectives, anti-proliferatives, anti-virals, (see column and column 13, lines 7-21 and 55-67). Pouyani et al. also teach of various ways these functionalized derivatives of hyaluronate may be administered, (see from column 14, line 35 to column 15, line 20). It is also noted that Pouyani et al. further teach that the hyaluronic acid gels may be used for cosmetic purposes, (see column 15, lines 48-50). Moreover, Pouyani et al. disclose of a process to

functionalized the hyaluronate by reacting hyaluronate with a dihydrazide while in the presence of carbodiimide, (see Scheme 1, column 4, lines 30-41). Pouyani et al. do not specifically teach of microspheres of hyaluronic acid; however, Pouyani et al. do state that functionalized hyaluronic acid compositions can be thought of as being composed of hydrophilic monomer units linked to form a soluble polymeric network and eventually crosslinked to form an insoluble network and that functionalized hyaluronic acid possesses a number of characteristics that make it advantageously used as a carrier of drugs, (see column 3, lines 44-51 and lines 60-65). The prior art reference of Kyyronen et al. teach of derivative microspheres of hyaluronic acid that are used to deliver a pharmaceutical, namely hydrocortisone, (see column 1, page 162). The determination of a dosage or a mode of administration having the optimum therapeutic index is well within the level of one having ordinary skill in the art, and the artisan would most certainly be motivated to determine optimum amounts and modes of administration in order to get the maximum effect of the drug while in the functionalized derivatives of hyaluronate. Accordingly, the references make obvious the instant invention.

Conclusion

16. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Wednesdays, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (571)-273-8300.

Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see http://pair-direct.uspto.gov. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

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DWAYNE JONES
PRIMARY EXAMINER

Tech. Ctr. 1614
February 9, 2005